Cylindrical Molecular Brushes of Poly(2-oxazoline)s from 2-Isopropenyl-2-oxazoline

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ABSTRACT: We report on the synthesis and characterization of cylindrical molecular brushes based on poly(2-oxazoline)s (POx). The dual-functional monomer, 2-isopropenyl-2-oxazoline (IPOx), was first converted to a poly(2-isopropenyl-2-oxazoline), backbone by free radical ($PIPOx^R$) or living anionic polymerization ($PIPOx^A$). Quantitative reaction with methyl triflate yields a macroinitiator salt ($PIPOxOTf^{R/A}$) for the preparation of molecular brushes via the grafting from approach by living cationic polymerization of 2-oxazolines (2-methyl-, 2-ethyl-, and 2-isopropyl-2-oxazoline). Characterization of the resulting molecular brushes by NMR and FTIR spectroscopy indicates a very high side chain grafting density and quantitative reactions. Visualization of adsorbed molecular brushes by AFM corroborates this assumption. Furthermore, the lower critical solution temperatures of the POx molecular brushes were determined. The transition temperatures were found to be very defined, reversible, and with no noticeable hysteresis.

Introduction

Molecular brushes[1] are linear macromolecules with pendant polymer side chains at high grafting densities—ideally at each backbone monomer unit. The side chain crowding induces a strong stretching of backbone and side chains, and the entire (cylindrical) molecular brush adopts an entropically unfavorable elongated shape.[2] Especially the possibility to visualize the single synthetic molecular brushes with scanning probe microscopy techniques triggered numerous contributions to synthesize defined molecular brushes and use the macromolecules as an individual device or as single molecule templates.[3−8]

As comb copolymers, molecular brushes can be prepared by the *grafting-through* approach (polymerization of macromonomers), *grafting-onto* approach (polymer analogue coupling of polymers onto a backbone with pendant attachment groups), or the *grafting-from* approach (polymerization from macroinitiators). All three strategies were successfully employed for the synthesis of defined molecular brushes; however, depending on the functionality and polarity of the monomers, each approach has its advantages and limitations.[1] For a defined synthesis of molecular brushes, mainly living ionic as well as controlled radical polymerization was used. However, also the facile free radical polymerization[2] results in reasonably defined molecular brushes. Although this approach is accompanied by the relatively broad molecular weight distributions of main or side chains, it is intriguing for future commercial applications of molecular brushes with respect to the bulk material science aspect.[9]

One focus of the related research on molecular brushes is the development of stimuli-responsive adaptive systems, e.g., hydrophilic molecular brushes with a lower critical solution temperature in aqueous environments due to the nature of the pendant side chains for i.e. biomedical applications.[8,10−16] In contrast to linear polymers, it was found that at temperatures above the LCST the molecular brushes collapse as individual molecules and not as aggregates.[8,17] As for aqueous solutions of linear polymers mainly oligo or poly(ethylene glycol) (PEG) and acrylates (i.e., poly(*N*-isopropylacrylaminde) (PNIPAAm)) were investigated, the projected use in the biomedical field will require a broader choice of adaptive molecular brushes to cope with the special requirements, namely toxicity and trafficking in complex biological environments.[18] Recently, hydrophilic poly(2-oxazoline)s (POx) came into focus as a potential alternative to the well-studied PEG systems.[19−22] Furthermore, the living cationic ring-opening polymerization (LCROP) of 2-substituted 2-oxazoline provides synthetic possibilities to tailor macromolecules with a broad variety of architectures, composition, and numerous side and end functions.[23−32] Additionally, the LCST of hydrophilic POx can be tailored over a broad temperature range.[33−39]

For the preparation of POx cylindrical molecular brushes all three routes (grafting-from, -through, or -to) are possible; however, e.g., the grafting through of POx macromonomers was employed with comonomers to realize sufficient degrees of polymerization.[40−44] Since POx is prepared by LCROP, it is of advantage to use the grafting-from approach, analogue to the surface-initiated polymerization of 2-oxazolines on surfaces or nanoparticles.[45,46] For the grafting-from approach, several synthetic strategies are possible. Kobayashi et al.[47] used hydroxyl groups of saponified poly[ethylene-*co*-(vinyl acetate)] to create pendant tosylate moieties for the grafting of POx side chains, and Nuyken et al.[48−51] used linear as well as (hyper)-branched macroinitiators containing benzyl chloride functions for the grafting of 2-oxazolines. Both approaches led to comb polymers with POx side chains of considerable grafting density. However, Nuyken et al. used statistical poly(isobutene-*co*-chloromethylstyrene) as the macroinitiator; thus, comblike polymers were obtained.

Here, we report on the synthesis of molecular brushes by the *grafting-from* method via combination of free radical or anionic polymerization of 2-isopropenyl-2-oxazoline to form the backbone and living cationic ring-opening polymerization of 2-alkyl-2-oxazolines from a polycationic macroinitiator to form the side chains.

Experimental Section

Materials and General Methods. Chemicals were purchased from Sigma-Aldrich (Steinheim, Germany) or Acros (Geel, Belgium) and were used as received unless otherwise stated. *N-tert*-Butyloxycarbonylpiperazine (*N*-Boc-pip) of highest available grade

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(>98%) was obtained from Sigma-Aldrich and used as received. Methyl triflate (MeOTf), 2-isopropenyl-2-oxazoline (IPOx), 2-methyl-2-oxazoline (MeOx), 2-ethyl-2-oxazoline (EtOx), 2-isopropyl-2-oxazoline (iPrOx), and acetonitrile (ACN) used for polymer synthesis were dried by refluxing over CaH_2 under a dry nitrogen atmosphere and subsequent vacuum distillation prior to use. NMR spectra were recorded on a Bruker ARX 300 at 292 K. The spectra were calibrated using the solvent signals ($CDCl_3$ 7.26 ppm, CD_3CN 1.94 ppm). FT IR spectra were obtained on a Bruker IFS 55s spectrometer with a MCT detector and a single bounce SplitPea-ATR sampling accessory from Harrick with a diamond crystal sampling unit at a spectral resolution of 4 cm^{-1}. Atomic force microscopy (AFM) scans were obtained with a Nanoscope IIIa scanning probe microscope from Veeco Instruments (Mannheim, Germany). The microscope was operated in tapping mode using Si cantilevers (tip radius was less than 10 nm) with a resonance frequency of 320 kHz and a driving amplitude of 1.25 V at a scan rate of 1.0 Hz. The polymers were diluted in chloroform ($c = 0.05$ mg/mL) and dip-coated on a clean silicon wafer piece and blew with nitrogen for ~1 min prior to the scanning. Gel permeation chromatography (GPC) was performed on a Waters system (pump model 510, RI detector model 410) using Resi Pore Guard (50 × 7.5 mm) and 2 × Resi Pore (300 × 7.5 mm) columns as the stationary and DMAc (75 mmol/L LiBr, $T = 80$ °C, 1 mL/min) as the mobile phase. The calculation of the average molar mass was performed using a calibration with PMMA standards from PSS (Mainz, Germany). Prior to the measurements, the polymer samples were dissolved in dimethylacetamide (DMAc) and filtered through 0.2 μm PTFE filters. Turbidity measurements were carried out on a Cary 3 UV−vis spectrophotometer from Varian. The cloud point was determined by spectrophotometric detection of the changes in transmittance at $\lambda = 500$ nm of the aqueous polymer solutions (1.0 wt %). The heating/cooling rate was 0.5 K min^{-1} followed by a 10 min period of constant temperature to ensure equilibration. Given values for the cloud point were determined as the temperature corresponding to a 10% decrease in optical transmittance.

Synthesis. *2-Isopropyl-2-oxazoline (iPrOx).* The monomer iPrOx was prepared according to a procedure we published recently.[52]

Polymerizations. *Radical Polymerization: Poly(2-isopropenyl-2-oxazoline), PIPOx^R.* Under a dry nitrogen atmosphere, 2-isopropenyl-2-oxazoline (IPOx) (1.00 g, 9.00 mmol) and AIBN (14.8 mg, 0.09 mmol) were heated to 60 °C for 8 h. Afterward, the reaction mixture was equilibrated to room temperature, diluted with chloroform (~15 mL), and precipitated into dry diethyl ether. The product was reprecipitated twice using chloroform and ether. After filtration and drying under vacuum, a colorless powder was obtained (0.5 g, yield = 50%). The obtained yield is typical for the free radical polymerization of IPOx as reported earlier by Fréchet et al.[53] ^{1}H NMR ($CDCl_3$): δ (ppm) 4.16 (br, 2H), 3.76 (br, 2H), 1.98−1.76 (br, 2H) and 1.24−1.12 (br, 3H). IR (ATR, film): 2941 (C−H str) (m), 1654 (C=N str) (vs), 1118 (C−O) (vs) (unconjugated), 986, 951 (vs) (ring skeletal vibration) cm^{-1}. GPC: PDI = 2.12, $M_n = 9800$ g/mol. Analysis of the ratio of α-methyl proton signals calculated to a tacticity ratio of syndiotactic (*S*):heterotactic (*H*):isotactic (*I*) of 57.0:37.2:5.8 (Figure 1).

Living Anionic Polymerization: Poly(2-isopropenyl-2-oxazoline), PIPOx^A. Adapting an early procedure of Tomalia et al.,[54] 3 mL of dry THF and 0.1 mL of a 2.5 M *n*-butyllithium solution in hexane (0.236 mmol, 1 equiv) were cooled under a dry argon atmosphere, to approximately −50 °C (acetone/dry ice). Over a period of 30 min, 1 mL (9.45 mmol, 40 equiv) of IPOx was added dropwise. After stirring the mixture for another 30 min at −50 °C, the mixture was equilibrated to room temperature and stirred again for 30 min. The polymer was end-capped by addition of 1 mL of methanol. The mixture was then precipitated using diethyl ether. After freeze-drying (water), 1.07 g (95% yield) of PIPOx^A was obtained as a colorless powder. ^{1}H NMR ($CDCl_3$): δ (ppm) 4.16 (br, 2H), 3.76 (br, 2H), 1.86−1.75 (br, 2H), 1.24−1.14 (br, 3H), and 0.85 (br, C_4H_9). IR (ATR, film): 2941 (C−H str) (m), 1654 (C=N str) (vs), 1118 (C−O) (vs) (unconjugated), 986, 951 (vs) (ring skeletal vibration) cm^{-1}. GPC: PDI = 1.20, $M_n = 24\,350$ g/mol. Analysis of the ratio of α-methyl proton signals calculated to a tacticity ratio of syndiotactic (*S*):heterotactic (*H*):isotactic (*I*) of 73.0:24.8:2.2 (Figure 1).

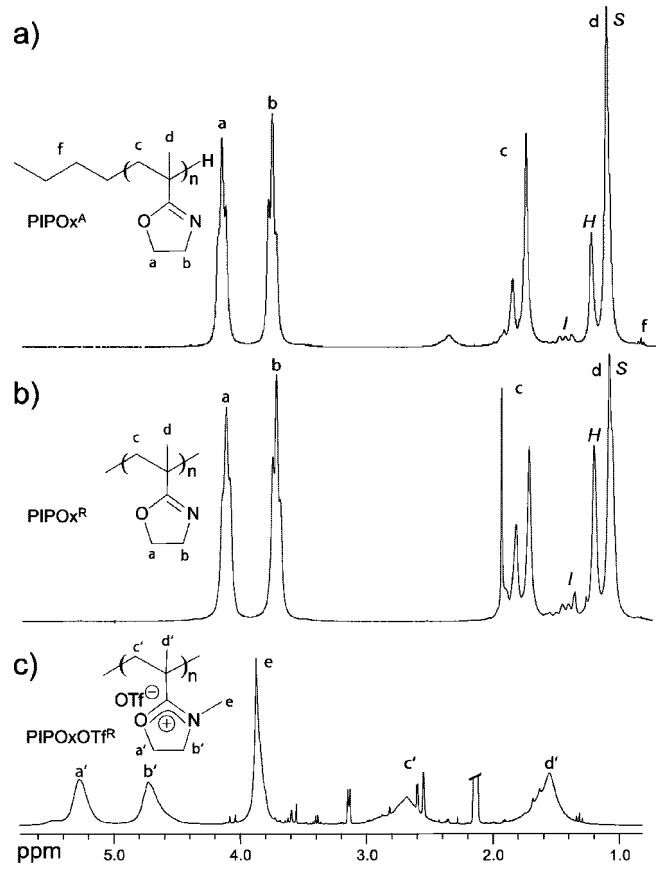


Figure 1. ^{1}H NMR spectra of (a) PIPOx^A, (b) PIPOx^R, and (c) PIPOxOTf^R along with the chemical structures and assignments. Neither the free radical nor the living anionic polymerization affected the integrity of the pendant 2-oxazoline ring. The new signal at 3.7 ppm and the quantitative shift of the two triplets from the pendant 2-oxazoline ring as well as the backbone signals (c, d to c′,d′) indicate a quantitative conversion to the polycationic macroinitiator PIPOxOTf. The intensity ratio of the α-methyl signals (d) at 1.12 ppm (syndiotactic, *S*), 1.24 ppm (heterotactic, *H*), and 1.39 ppm (isotactic, *I*) was used to determine the polymer tacticity.

Macroinitiator Salt: Poly(2-isopropenyl-2-oxazolium triflate), PIPOxOTf$^{R/A}$. Under dry and inert conditions, PIPOx^A (222 mg, 1.0 equiv of oxazoline unit) and 394 mg (2.4 mmol, 1.2 equiv) of MeOTf were added to 5 mL of dry acetonitrile at approximately −35 °C. After stirring for 5 h at 0 °C, the mixture was poured into cold and dry diethyl ether to precipitate the oxazolinium salt. The colorless precipitate was washed twice with cold ether to yield 529 mg (1.92 mmol, 96%). PIPOxOTf^R was obtained in an analogue procedure with a yield of 95%. ^{1}H NMR (CD_3CN): δ (ppm) 5.08 (br, 2H, =N−CH_2−CH_2−O−), 4.54 (br, 2H, =N−CH_2−CH_2−O−), 3.70 (s, 3H, CH_3−N), 2.49 (2H, −C−CH_2−), 1.36 (br, 3H, −C−CH_3).

Poly(2-isopropenyl-2-oxazoline-g-2-methyl-2-oxazoline), P(IPOx-g-MeOx)^R. At 0 °C, PIPOxOTf^R (110 mg, 0.4 mmol, 1.0 equiv) was dissolved in 10 mL of acetonitrile, and 850 mg of 2-methyl-2-oxazoline (MeOx) (10 mmol, 25 equiv) was added. The polymerization solution was heated by a prepared oil bath to 85 °C and stirred for 20 h. The mixture was cooled to 0 °C, and 298 mg (1.6 mmol, 4 equiv) of *N-tert*-butyloxycarbonylpiperazine (N-Boc-pip) was added. After stirring the reaction mixture for 4 h at room temperature, an excess of finely grounded potassium carbonate (~60 mg) was added, and the mixture was allowed to stir overnight. The solvent was removed under reduced pressure, and the residual dissolved in ~15 mL of chloroform and then precipitated three times into dry diethyl ether. The product was freeze-dried (water)

to yield a colorless powder (860 mg, 80% yield). Additionally, the product was purified by column chromatography using Sephadex G100 to quantitatively separate the product from minor portions of homopolymer side products. ^{1}H NMR (CD_3Cl): δ (ppm) 3.44 (br, 82H, $-N-CH_2-CH_2-N-$) 2.13/2.07 (m, 57H, $-CO-CH_3$), 1.98/1.92 (br, 2H, CH_2-C) 1.46/1.44 (br, 12H, CH_3^{Boc} and CH_3-C). IR (ATR, film): 2939 (C−H str) (m), 1696 (C═O str, ester), 1629 (C═O str, amide I) (vs), 1419 $\delta(CH_2-CO)$ (s), 731 cm^{-1} r(CH_2) (w). GPC: PDI = 1.69, M_n = 69 500 g/mol.

Poly(2-isopropenyl-2-oxazoline-g-2-ethyl-2oxazoline), P(IPOx-g-EtOx)^R. As described above, P(IPOx-*g*-EtOx)^R was obtained using 110 mg of PIPOxOTf^R, 990 mg of 2-ethyl-2-oxazoline (EtOx), and 298 mg of *N*-Boc-pip. The polymerization time was 30 h. After column chromatography and freeze-drying, a colorless powder was obtained (940 mg, 76% yield). ^{1}H NMR (CD_3Cl): δ (ppm) 3.44 (br, 86H, $-N-CH_2-CH_2-N-$) 2.39 (br, 41H, $-CO-CH_2CH_3$), 1.98/1.92 (br, 2H, $-CH_2-C$), 1.46/1.44 (br, 12H, CH_3^{Boc} and CH_3-C), 1.10 (br, 62H, $-CO-CH_2CH_3$). IR (ATR, film): 2937 (C−H str) (m), 1699 (C═O str, ester), 1629 (C═O str, amide I) (vs), 1428 $\delta(CH_2-CO)$ (s), 731 cm^{-1} r(CH_2) (w). GPC: PDI = 1.75, M_n = 77 500 g/mol.

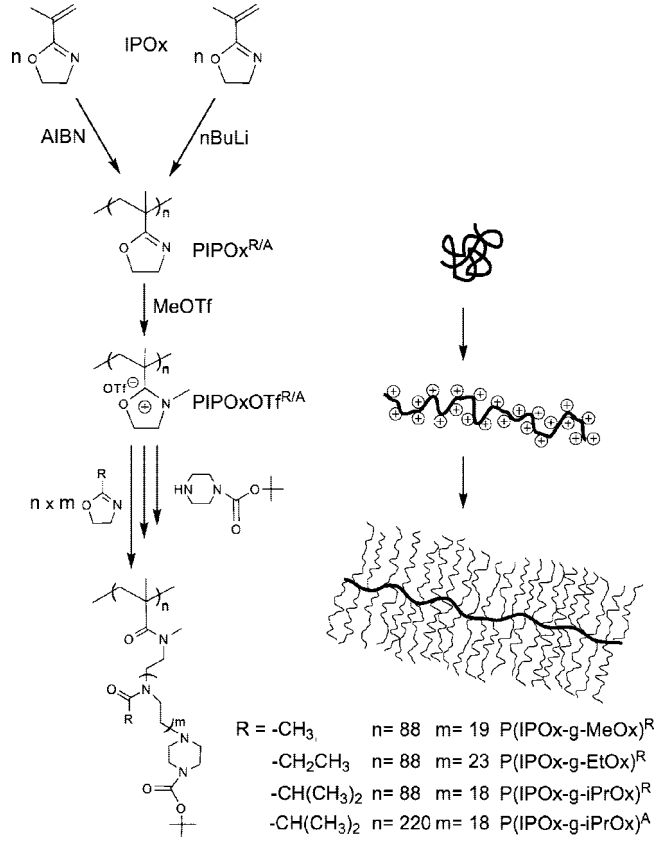
Poly(2-isopropenyl-2-oxazoline-g-2-isopropyl-2-oxazoline), P-(IPOx-g-iPrOx)^R. Following the procedure described above, P(IPOx-*g*-iPrOx)^R was obtained using 110 mg of PIPOxOTf^R, 1.13 g of iPrOx, and 298 mg of *N*-Boc-pip. The polymerization time was 40 h. After freeze-drying (water), a colorless powder was obtained (630 mg, 50% yield). In this case, no homopolymer side product could be detected. ^{1}H NMR (CD_3Cl): δ (ppm) 3.45 (br, 72H, $-N-CH_2-CH_2-N-$) 2.88 (br, 22H, $-CO-CH(CH_3)_2$), 1.98/1.92 (br, 2H, CH_2-C), 1.46/1.45 (br, 12H, CH_3^{Boc} and CH_3-C), 1.09 (br, 105H, $-CH(CH_3)_2$). IR (ATR, film): 2937 (C−H str) (m), 1698 (C═O str, ester) 1637 (C═O str, amide I) (vs), 1419 $\delta(CH_2-CO)$ (s), 731 cm^{-1} r(CH_2) (w). GPC: PDI = 1.58, M_n = 53 200 g/mol.

Poly(2-isopropenyl-2-oxazoline-g-2-isopropyl-2-oxazoline), P-(IPOx-g-iPrOx)^A. Following the procedure described above, P(IPOx-*g*-iPrOx)^A was obtained accordingly (49% yield). Also in this case, no homopolymer side product could be detected. ^{1}H NMR (CD_3Cl): δ (ppm) 3.45 (br, 76H, $-N-CH_2-CH_2-N-$) 2.88(br, 23H, $-CO-CH(CH_3)_2$), 1.98/1.92 (br, 2H, CH_2-C), 1.46/1.45 (br, 12H, CH_3^{Boc} and CH_3-C), 1.09 (br, 110H, $-CH(CH_3)_2$). IR (ATR, film): 2937 (C−H str) (m), 1698 (C═O str, ester) 1637 (C═O str, amide I) (vs), 1419 $\delta(CH_2-CO)$ (s), 731 cm^{-1} r(CH_2) (w). GPC: PDI = 1.33, M_n = 125 000 g/mol.

Results and Discussion

The monomer 2-isopropenyl-2-oxazoline (IPOx) has two orthogonal polymerizable groups, namely a vinyl group for the free radical or living anionic polymerization and the 2-oxazoline ring for the living cationic ring-opening polymerization (LCROP). It was shown that conversion of the vinyl group to poly(2-isopropenyl-2-oxazoline) (PIPOx) by radical[52,55−57] as well as anionic[53] polymerization does not affect the 2-oxazoline ring. Hence, the preparation of POx molecular brushes is straightforward: first, a conversion of the vinyl group by free radical or anionic polymerization to form the molecular brush backbone and, second, a *grafting-from* reaction using 2-oxazolines by LCROP. For the latter the PIPOx has to be converted to a macroinitiator salt with pendant oxazolinium rings by the reaction with a stochiometric amount of methyl triflate (MeOTf). This approach has the advantage that a robust but very effective macroinitiator[58] is formed with equal reactivities as compared to e.g. the moisture-sensitive triflates or tosylates.[59] Furthermore, the charging of each monomer unit along the PIPOx chain to a polyelectrolyte induces significant chain stretching which improves the accessibility of the initiation sites along the main chain for the 2-oxazoline monomers. Especially for grafting by ionic living polymerization, a fast initiation reaction is crucial to obtain side chains of low polydispersities. Both aspects, macroinitiator chain stretching and the formation of the oxazolinium salt, work in favor for a fast initiation reaction of the LCROP for a defined side chain grafting. As outlined in the reaction pathway (Scheme 1), we synthesized molecular brushes with three different types of side chains. While 2-methyl-2-oxazoline (MeOx) will give very hydrophilic brushes, 2-ethyl-2-oxazoline (EtOx) and 2-isopropyl-2-oxazoline (iPrOx) are converted to monomer units of slight amphiphilicity, and the resulting polymers are known to show a sharp LCST.[33−51]

Scheme 1. Synthesis of Molecular Brushes by Radical as Well as Living Anionic Polymerization of 2-Isopropenyl-2-oxazoline (IPOx) for the Backbone, Conversion to the Macroinitiator Salt (PIPOx$^{R/A}$), and Formation of Poly(2-oxazoline) Pendant Chains by Living Cationic Polymerization of Different 2-Alkyl-2-oxazoline)s (2-Methyl-2- (MeOx), 2-Ethyl-2- (EtOx), and 2-Isopropyl-2-oxazoline (iPrOx))



As outlined in Scheme 1, we prepared the molecular brush backbone by free radical as well as living anionic polymerization. While the latter gives narrow molar mass distributions and thus a better overall definition of the resulting molecular brushes, the free radical polymerization of IPOx is facile, straightforward, and better suitable for large-scale production. An alternative would be to use controlled radical polymerization. However, our initial attempts to convert IPOx by atom transfer radical polymerization were not successful. Only oligomeric products were obtained due to a strong complexation of copper by the pendant 2-oxazoline units of oligomers.The results of the radical and anionic polymerization of IPOx and the grafting from polymerization of 2-alkyl-2-oxazolines by LCROP using the macroinitiator salt are summarized in Table 1.

As reported earlier,[52−55] the free radical polymerization of IPOx using AIBN resulted in hydrophilic PIPOx^R with a typical molecular weight distribution of PDI = 2.1 while the anionic polymerization resulted in PIPOx^A with a PDI of 1.2. In contrast to the early report from Tomalia et al.,[53] higher degrees of polymerization at relatively low molar mass distributions could be obtained. However, the PDI of 1.2 indicates that the anionic polymerization is accompanied to some extent by i.e. termina-

Table 1. Synthesized Poly(2-oxazoline) Macroinitiators and Molecular Brushes

polymer	yield (%)	M_n (kg/mol)[b]	PDI[b] (M_w/M_n)	n^b	m^c	m^{theor}
$PIPOx_n^R$	50[a]	9.8	2.12	88		
$PIPOx_nOTf^R$	96					
$P(IPOx_n\text{-}g\text{-}MeOx_m)^R$	80	70	1.69	88	19	25
$P(IPOx_n\text{-}g\text{-}EtOx_m)^R$	76	78	1.75	88	23	25
$P(IPOx_n\text{-}g\text{-}iPrOx_m)^R$	50[d]	53	1.58	88	18	25
$PIPOx_n^A$	95[a]	24	1.20	220		
$P(IPOx_n\text{-}g\text{-}iPrOx_m)^A$	49[d]	125	1.33	220	18	25

[a] Calculated against initial initiator feed. [b] As calculated from GPC traces. [c] Average degree of polymerization (m) calculated from end-group analysis using ^{1}H NMR spectral data. [d] Note: the lower yields are due to the loss of material during purification.

tion/chain transfer via H^+ abstraction. The estimation of the average degree of polymerization based on gel permeation chromatography data (with PMMA standards for calibration) appears to be quite accurate. The complementary end-group analysis of $PIPOx^A$ based on ^{1}H NMR data using the signals at 0.9 ppm (9H) of the terminal butyl group versus the signals of the monomer units resulted in a similar value of $n = 220$.

For both PIPOx polymers, analysis of the ^{1}H NMR spectra confirmed that the pendant 2-oxazoline rings were preserved (Figure 1). The integral ratio of the ring methylene groups (a, 2H and b, 2H) and the corresponding signal integrals of the polymer backbone (c, 2H; d 3H) is in excellent agreement and confirms the depicted polymer structure. Closer inspection of the proton backbone signals (c, d) in Figure 1 also reveals a fine structure due to the tacticity of PIPOx.[54] Similar to PMMA,[60] the tacticity of PIPOx can be estimated from the relative intensity of the characteristic α-methyl signals for syndio (*S*) (1.12 ppm), hetero (*H*) (1.24 ppm), and isotactic (*I*) (1.39 ppm) polymer sequences. For $PIPOx^R$ an *S:H:I* ratio of 57:37:6 and for $PIPOx^A$ a ratio of 73:25:2 were found. The determined *S:H:I* ratio for $PIPOx^R$ is in agreement with earlier findings by Kagiya et al.[54] The living anionic polymerization of IPOx results in $PIPOx^A$ with a significant larger syndiotactic and lower isotactic fraction. This can be explained by the steric demand of the pendant 2-oxazoline ring during the slower anionic chain reaction.

The polycationic macroinitiator salts, $PIPOxOTf^{R/A}$, were prepared from $PIPOx^{R/A}$ and methyl triflate (MeOTf). Exemplarily, the ^{1}H NMR spectrum of $PIPOxOTf^R$ is shown in Figure 1. Upon methylation, a new signal of the *N*-methyl group at 3.7 ppm appears, and the characteristic two triplet signals of the 2-oxazoline methylene protons at 3.76 and 4.16 ppm are quantitatively shifted to 4.54 and 5.08 ppm. The ratio of the intensities of the new *N*-methyloxazolinium ring and the methyl signals is again in excellent agreement with signal intensities originating from the backbone protons. Based on NMR spectral analysis, the conversion of $PIPOx^R$ to the macroinitiator salt, $PIPOxOTf^R$, was quantitative. For $PIPOx^A$ (data not shown) the same quantitative conversion was found.

However, in the spectrum of the macroinitiator some low molar mass impurities are noticeable. First attempts to remove these impurities resulted in minor but noticeable reaction of the oxazolinium rings (e.g., hydrolysis). Thus, we used $PIPOxOTf^{R/A}$ as obtained after a single precipitation and washing step to initiate the side-chain grafting from polymerization of 2-methyl-, 2-ethyl-, and 2-isopropyl-2-oxazoline by LCROP. The targeted length of the side chains was set to $m = 25$ by the initial $[M]_0/[I]_0$ ratio. Analogue to our previous accounts on functionalized POxs, *N*-Boc-piperazine (*N*-Boc-pip) was used as the terminating reagent. This terminal group is useful for ^{1}H NMR end-group analysis, and moreover, after deprotection of the secondary amine group, it allows for an additional functionalization of each side chain end.[22,58,61−64] First, the molecular brushes

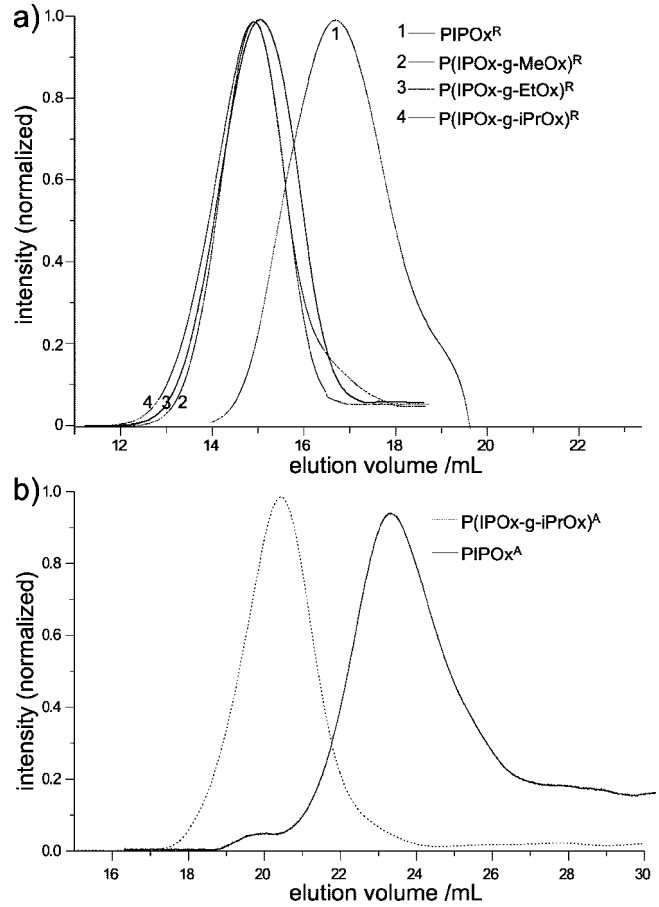


Figure 2. GPC traces of (a) $PIPOx^R$ and molecular brushes $P(IPOx\text{-}g\text{-}MeOx)^R$, $P(IPOx\text{-}g\text{-}EtOx)^R$, and $P(IPOx\text{-}g\text{-}iPrOx)^R$. (b) $PIPOx^A$ and $P(IPOx\text{-}g\text{-}iPrOx)^A$.

were analyzed by GPC. For all four graft copolymers a significant increase of the molar mass was observed with no remaining macroinitiator. In all cases a monomodal elution curve was obtained with no fractions of polymers having lower molar masses.

Because of the side-chain grafting for $PIPOxOTf^R$, the number-average molar mass increased to $M_n = 7 \times 10^4$, 8×10^4, 5×10^4 g/mol for MeOx, EtOx, and iPOx, respectively. The macroinitiator prepared by living anionic polymerization, $PIPOxOTf^A$, yielded a graft copolymer, $P(IPOx\text{-}g\text{-}iPrOx)^A$, with $M_n = 1.2 \times 10^5$ g/mol. In Figure 2, the GPC traces of $PIPOx^R$ and $PIPOx^A$ are compared with the traces of the resulting molecular brushes.

The successful side chain formation from the macroinitiators by the grafting from approach was confirmed by ^{1}H NMR spectroscopy (Figure 3). For all grafting polymerization it was observed that the signals corresponding to the oxazolinium pendant group disappeared completely, and instead, characteristic signals for the respective side chain polymers could be unambiguously assigned. Furthermore, a successful functionalization by *N*-Boc-pip via the termination reaction is confirmed by the presence of a strong signal around 1.45 ppm originating from the *tert*-butyl group (overlapping with the α-methyl signals of the brush backbone). Estimation of the average degree of polymerization, *m*, of the POx side chains was performed by comparing the signal integral of the *tert*-butyl group and the α-methyl signals at 1.45 ppm of the brush backbone versus the methylene signal of the POx side chain at 3.45 ppm. Although a targeted degree of polymerization of $m = 25$ for the side chains, in all cases slightly shorter chains of about $m = 20$ were determined (Table 1). An incomplete grafting from or termina-

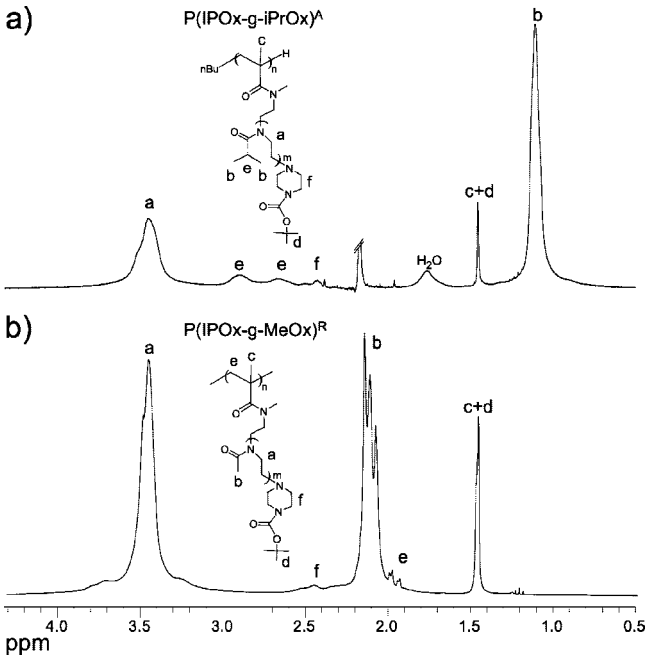


Figure 3. ^{1}H NMR spectra of the molecular brushes (a) P(IPOx-*g*-iPrOx)^A and (b) P(IPOx-*g*-MeOx)^R with their assignments. Besides the characteristic backbone and POx monomer unit signals (a, b), end-group signals (d, f) are detectable.

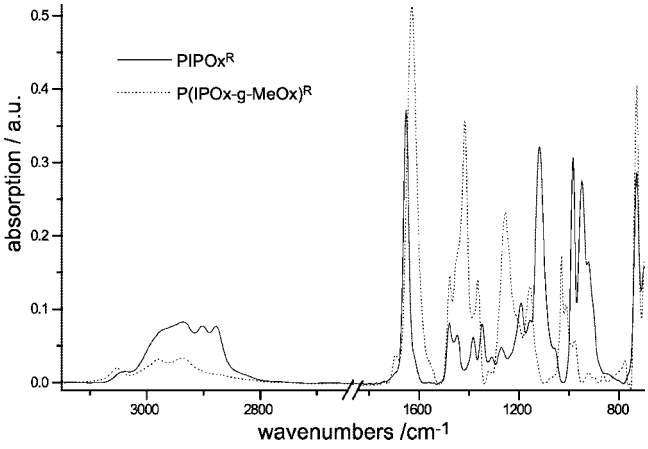


Figure 4. FTIR spectra of PIPOx^R (solid line) and the molecular brush P(IPOx-*g*-MeOx)^R (gray dashed line).

tion reaction would calculate to longer side chains. Thus, this result indicates a very high grafting density (within experimental error, 100%) and efficient end-group functionalization via the termination reaction. The resulting shorter side chains may be caused by chain transfer reactions or, more likely, residual MeOTf in the macroinitiator salt. In fact, for the grafting of MeOx and EtOx minor amounts of homopolymer were observed that we attribute to traces of MeOTf in the macroinitiator. However, to ensure a homogeneous and high grafting density along the polymer backbone, we decided to avoid elaborate cleaning procedures of the macroinitiator.

Further confirmation for the successful grafting of POxs from the macroinitiator salts was obtained by FTIR spectroscopy. Exemplarily, in Figure 4, the IR spectra of PIPOx^R and P(IPOx-*g*-MeOx)^R are compared.

The strong bands at 1654 and 1118 cm^{-1} are assignable to the (C═N) and (C−O) moieties and the bands at 986 and 951 cm^{-1} originate from the ring skeletal vibration of the pendant 2-oxazoline rings and in PIPOx^R. After ring-opening polymerization, these bands disappeared completely, and a new sharp and intensive band appeared around 1630 cm^{-1} which is characteristic for the carbonyl stretching mode of the amide function (amide I)[32,44,58] and confirms the successful grafting by LCROP to P(IPOx-*g*-MeOx)^R. Moreover, the characteristic CH_x stretching pattern between 2800 and 3200 cm^{-1} and the CH_x deformation modes for POxs observed between 1365 and 1477 cm^{-1} as well as the carbonyl stretching vibration of the Boc group are found in the spectrum.

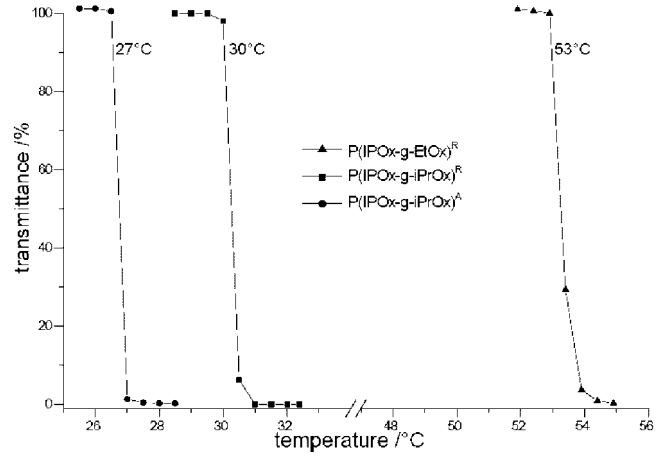


Figure 5. Determination of the LCST of P(IPOx-*g*-EtOx)^R, P(IPOx-*g*-iPrOx)^R, and P(IPOx-*g*-iPrOx)^A, determined by turbidity measurements of a 1.0 wt % aqueous polymer solution. Only heating curves are shown; upon cooling the same transition point was found with no noticeable hysteresis.

Thermoresponsiveness of Poly(2-oxazoline) Molecular Brushes: LCST. The hydrophilicity of the molecular brushes is determined by the length of the alkyl group in the 2-position of the respective oxazoline monomers forming the side chains. Longer pendant alkyl chains of the monomer unit results in an increasingly stronger amphiphilic character of the monomer unit and the polymer becomes a nonionic polysoap.[60,65,66] As most of the water-soluble polymers,[67] hydrophilic POxs have a lower critical solution temperature (LCST), above which the polymer becomes water-insoluble. Taking advantage of the flexibility of the 2-oxazoline chemistry and the LCROP giving access to defined (co)polymers having various side and end groups, recent studies by Kataoka and us demonstrated the fine-tuning of the LCST of POxs over a broad temperature range.[36−38,51] Until now, the LCST of hydrogels and linear POx homo- and copolymers were investigated in detail as a function of the side chain and/or end-group functionality as well as the molar mass and concentration.[34,35,68] Here, we present the temperature-dependent water solubility of the new POx molecular brushes. The LCST was determined analogue to our previous accounts[38,51] by turbidity measurements of a 1.0 wt % aqueous solution of P(IPOx-*g*-EtOx)^R, P(IPOx-*g*-iPrOx)^R, and P(IPOx-*g*-iPrOx)^A. The results are summarized in Figure 5. P(IPOx-*g*-MeOx)^R was too hydrophilic and thus water-soluble to a temperature close to the water boiling point.

For all three polymer brush solutions, the LCST transition was found to be very sharp; i.e., the complete transition occurred within a temperature range of $T = 0.5-1.5$ °C. Furthermore, repetitive measurements showed that the transitions were fully reversible, with no remaining insoluble polymer fraction below the respective LCST. The LCST of P(IPOx-*g*-EtOx)^R was found to be about 53 °C, which is significantly lower than the LCST between 73 and 69 °C found for linear poly(2-ethyl-2-oxazline) with comparable high molar mass as reported by Du Prez et al.[34] For the molecular brushes with P(iPrOx) side chains transition temperatures at 30 °C for P(IPOx-*g*-iPrOx)^R and 27 °C for P(IPOx-*g*-iPrOx)^A were determined. Also in this case, the LCST is significantly lower than the earlier reported values

Table 2. Summary of LCST Measurements of Investigated Polymers and Comparison of Thermal Behavior with Corresponding Linear Polymers

	$P(IPOx_n\text{-}g\text{-}EtOx_m)^R$	$P(IPOx_n\text{-}g\text{-}iPrOx_m)^R$	$P(IPOx_n\text{-}g\text{-}iPrOx_m)^A$	$P(IPOx_n\text{-}g\text{-}iPrOx_m)^R$ (without Boc)
LCST (°C)	53	30	27	53
width of transition[a] (°C)	1.5	1	0.5	7
LCST of linear polymer[b] (°C)	69[34]	36 (M_n = 16.7 kg/mol)[69]	n.a.[c]	n.a.[c]

[a] Temperature range between 100% and ~0% transmittance. [b] Of comparable molar mass. [c] We were unable to find references that studied 2-isopropyl-2-oxazoline-based polymers of comparable molar mass.

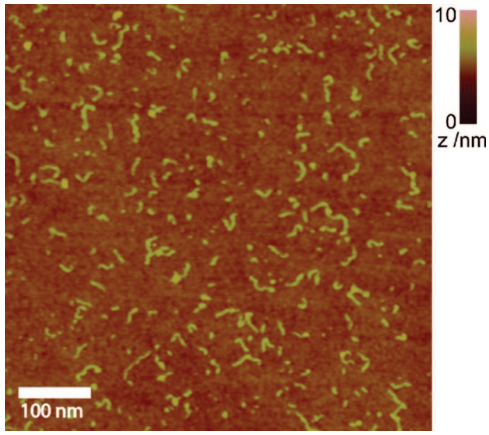


Figure 6. AFM scan of the molecular brush $P(IPOx\text{-}g\text{-}EtOx)^R$. The polymer was deposited by dip-coating from a dilute chloroform solution onto an oxidized silicon surface.

for linear PiPrOx (35−45 °C)[36,37,69] as well as cross-linked PiPrOx hydrogels (Table 2). For thermosensitive molecular brushes, the unique molecular architecture has only minor effects upon the value of the LCST.[8,11,12] The observed differences are explained by the end functionalization of the POx pendant chains with a *tert*-butyl group. As recently reported, the impact of the polarity of the POx end group upon the LCST modulation was found to be significantly stronger as compared to e.g. the well-known poly(*N*-isopropylacrylamide). In fact, after deprotection of $P(IPOx\text{-}g\text{-}iPrOx)^R$ using trifluoroacetic acid resulting in terminal secondary amide end groups of each polymer side chain, the LCST of the POx brush was shifted by 23 °C to 53 °C. Also, this indicates a high end-group functionality of the polymer pendant chains.

Comparing the molecular brushes $P(IPOx\text{-}g\text{-}iPrOx)^R$ and $P(IPOx\text{-}g\text{-}iPrOx)^A$ with the same composition but different length of the brush backbone, a decrease of the backbone length results in a higher LCST. Interestingly, the less structurally defined $P(IPOx\text{-}g\text{-}iPrOx)^R$ showed an LCST transition as sharp as for the defined $P(IPOx\text{-}g\text{-}iPrOx)^A$.

Morphology of Adsorbed POx Molecular Brushes. The ^1H NMR spectroscopy data indicate that the grafting-from reactions from the macroinitiator salts are quantitative, and molecular brushes with very high grafting densities were formed. This would result in cylindrical molecular brushes with a strongly stretched polymer brush backbone.[1,3,6] To investigate the overall molecular shape of the synthesized molecular brushes, atomic force microscopy (AFM) was used to visualize the individual molecules deposited on naturally oxidized silicon substrates from a dilute solution. In Figure 6 the AFM measurement of $P(IPOx\text{-}g\text{-}EtOx)^R$ is shown. The individual molecular brushes could be successfully visualized and display the characteristic shape of strongly stretched chains. Clearly, the length of the polymer brushes varies considerably because of the synthetic route used.

Conclusions

Poly(2-oxazoline) cylindrical molecular brushes were prepared from the dual-functional monomer, 2-isopropenyl-2-oxazoline (IPOx). While the combination of living anionic and living cationic ring-opening polymerization (LCROP) yields defined molecular brushes with an overall polydispersity index of 1.3, also the free radical polymerization/LCROP route proofed to be versatile to obtain molecular brushes of the required dense side chain grafting density. The intermediate step to form a polycationic macromolecular initiator salt is favorable for high grafting efficiency for the second grafting-from reaction of 2-oxazolines. As judged from the analysis by NMR and FTIR spectroscopy, macroinitiator salt formation as well as the ring-opening living polymerization is quantitative. The resulting polymers are of cylindrical shape with a strongly stretched polymer backbone. With poly(2-ethyl- and 2-isopropyl-2-oxazoline) side chains, the molecular brushes display a sharp, reversible LCST in aqueous solutions. Currently, the synthesis and physical properties of POx molecular brushes with a variety of different side chain compositions and functions are under investigation in our laboratories.

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